Journal of Research in Pharmacy Practice

Brief Communication

# The effect of pseudocatalase/superoxide dismutase in the treatment of vitiligo: A pilot study

**Farahnaz Fatemi Naini[1,2,3], Alireza Vaez Shooshtari[2,3], Bahareh Ebrahimi[2], Razieh Molaei[4]**

[1]Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran

[2]Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Department of Dermatology, Isfahan University of Medical Sciences, Isfahan, Iran

[4]Cell and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

**Received:** June 2012
**Accepted:** September 2012

**Corresponding author:**
Dr. Bahareh Ebrahimi,
**E-mail:** dr.bebrahimi@yahoo.com

## ABSTRACT

**Objective:** Pseudocatalase/superoxide dismutase (PSD) is a topical gel considered having therapeutic effects in vitiligo. This study was designed to evaluate the efficacy of this combination in vitiligo.

**Methods:** This was a pilot randomized, double-blind, placebo-controlled trial on 46 symmetrical vitiligo lesions of limbs in 23 patients referring to dermatology clinics, Isfahan, Iran in 2010. Patients were received this formula or placebo gels for the right and left lesions. Lesion area and degree of pigmentation were assessed at baseline, 2, 4, and 6 months.

**Findings:** There were no significant changes in lesion area and perifollicular pigmentation in each group ($P > 0.05$).

**Conclusion:** The results indicated no significant therapeutic effect for PSD in vitiligo.

**Keywords:** Pseudocatalase/superoxide dismutase; efficacy; vitiligo

## INTRODUCTION

Vitiligo, a common depigmenting skin disease, affects approximately 0.5% of population worldwide.[1] It is considered to be a multifactorial disease. These factors include autoimmune, biochemical, oxidant–antioxidant, and neural ones.[2]

Several repigmenting methods including non-surgical and surgical ones have been evaluated for vitiligo. Non-surgical therapies include phototherapy, laser, and topical medications such as corticosteroids, antioxidants, immunomodulators, prostaglandin E, and vitamin D derivatives. Surgical therapy consists of the use of autologous skin grafts.[1-4]

One recent theory in the pathophysiology of vitiligo is oxidative stress and accumulation of hydrogen peroxide ($H_2O_2$) in epidermal layer of depigmented area. High level of $H_2O_2$ in the epidermis is toxic for melanocytes, inhibits tyrosinase and also deactivate catalase which is a peroxisomal enzyme catalyzing the reduction of $H_2O_2$ to water and oxygen. Such imbalance between oxidative damage and antioxidant enzyme systems has an important role in melanocyte destruction.[2,5,6] Some investigators tried to replace the impaired catalase with a "pseudocatalase," a complex which is activated by ultraviolet B (UVB) radiation or natural sun. Till now, many studies have been conducted to show the usefulness of this regime, although some of which failed to show such result.[7-10]

Inasmuch as there are controversial results on the effectiveness of pseudocatalase cream in vitiligo treatment, this study was conducted to determine the efficacy of a formulation containing *Cucumis melo* superoxide dismutase (SOD) and catalase in the treatment of vitiligo.

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## METHODS

This pilot randomized, matched-paired, double-blind, placebo-controlled trial was performed in outpatient dermatological clinics in Isfahan, Iran in 2010. Inclusion criteria included having bilateral vitiligo for at least 12 months, no white hair on depigmented lesions, and no perifollicular pigmentation. Those who had unstable vitiligo, thyroid disease, and diabetes mellitus or have had any topical or systemic therapy within the last 4 weeks were not included in this study. Considering $\alpha = 0.05$, study power = 80%, and expected improvement for pseudocatalase/superoxide dismutase (PSD) as 63% versus 20% for placebo, the sample size for each group was calculated as 21 lesions. These 21 patients were selected consecutively and each patient acted as his/her own control. Ethical approval based on the Declaration of Helsinki was obtained from the Isfahan University of Medical Sciences Ethics Committee and all subjects gave written informed consent.

Two similar square-shaped lesions in the limbs, one on right side and the other on the inverse side, were selected to apply either placebo or PSD gel. Patients were alternately allocated to receive PSD or placebo gels for the right and left lesions, respectively, by a pharmacist. The PSD gel and the placebo were provided by the manufacturer (Life Science Investments Ltd, London, UK) in a 3.2-kg container. The PSD and placebo gel were packed and coded in identical containers for each patient by a pharmacist. Therefore, patients, corresponding physicians, and investigators were all blinded to the group assignment till the end of the trial.

During the initial visit, a detailed history was taken by the investigator and the extent of each vitiligo lesion area was assessed manually. The patients were asked to apply topical treatments (one gel for each side) to the absolutely clean affected skin twice daily and massage slightly to allow it to penetrate the skin. Also, patients were advised to have sun exposure for at least 30 min between 11 am and 2 pm daily without sun screen or make-up. They were asked to stop application of the mentioned medications and call the physician in case of any adverse or allergic reaction within 24 h of first application of the gels. The treatment lasted for 6 months and every 2 months, the reassessment visit was done by the investigator. The extent of each vitiligo lesion area was assessed as following: The patient was asked to figure out the affected site of body in defined and specific position. Then, this position was recorded in his/her follow-up paper to figure out the same position in next assessment session in order to have precise measurement of each vitiligo lesion. The lesion's area was calculated as multiplying the longest length of each lesion to the longest width of it. Also, the scoring of perifollicular pigmentation was as following: (1) No perifollicular pigmentation; (2) perifollicular pigmentation <25% of lesion area; (3) perifollicular pigmentation 25-50% of lesion area; and (4) perifollicular pigmentation >50% of lesion area. Moreover, all adverse events were recorded.

Data were analyzed with SPSS software version 15 (SPSS® Inc, Chicago, IL, Usa). A repeated measurment analysis was used to evaluate the changes in the mean extent of vitiligo lesions' area before and after treatments. A *P* value of <0.05 was considered statistically significant for all analyses.

## RESULTS

Twenty-three patients (20 women and 3 men) with bilateral vitiligo lesions were enrolled into this trial. The mean extent of vitiligo lesions' area at baseline and all reassessment visits after treatment with PSD and placebo are shown in Table 1.

According to repeated measurement analysis, the decrease in the mean extent of vitiligo lesions' area was not statistically significant during the study period in both the groups. Also, no significant differences were seen between treatment with PSD and placebo at baseline and all reassessment visits [Figure 1].

No side effect was seen in none of the groups. The score of perifollicular pigmentation in each group was 1 at baseline and no change was occurred during the study in it.

## DISCUSSION

This pilot study showed insignificant repigmentation

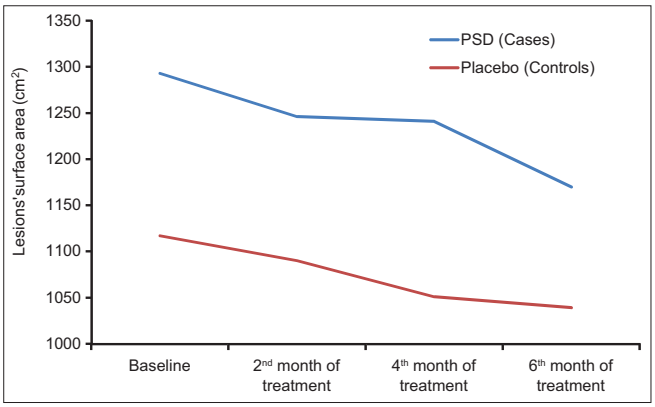


**Figure 1:** Changes of the extent of vitiligo lesions' area during the study in two groups, PSD: Pseudocatalase/superoxide dismutase

**Table 1: The mean extent of vitiligo lesions' area (mean±standard deviation) at baseline and all reassessment visits after the treatment with pseudocatalase/superoxide dismutase and placeb**

| Visit intervals | Surface area of the vitiligo lesions ($cm^3$) | | *P values |
|---|---|---|---|
| | PSD treatment group | Placebo group | |
| Baseline measurement | 1,293±2,120 | 1,117±1,614 | 0.75 |
| Two months after treatment | 1,246±2,121 | 1,090±1,611 | 0.78 |
| Four months after treatment | 1,241±2,031 | 1,051±1,519 | 0.72 |
| Six months after treatment | 1,170±1,861 | 1,039±1,518 | 0.79 |
| *P value | 0.162 | 0.151 | |

*Repeated measure test, PSD: Pseudocatalase/superoxide dismutase

of vitiligous lesions treated with a formulation of SOD and catalase in comparison with placebo. It is considered that oxidative stress is the initial step in melonocyte destruction. Some studies found the increased activity of SOD, which dismutates the anion to form $O_2$ and $H_2O_2$ in vitiligo patients. In this case, catalase is needed to convert $H_2O_2$ to $O_2$ and $H_2O$. In the presence of high level of $H_2O_2$, which was showed in vitiligo patients in some studies, SOD is increased but catalase level and activity are decreased. On the other hand, the level of nitric oxide (NO), which inhibits $H_2O_2$ catabolism, increased in these patients. The production of NO is inhibited by catalase too. These events lead to a defective cycle and as a result destruction of more and more melanocytes.[5,6]

A plant extract formulation from *C. melo*, SOD and catalase (Vitix®, Life Science Investments Ltd, London, UK), has been introduced for vitiligo patients. It is claimed that this medication can be beneficial for the removal of the $H_2O_2$ from the skin and consequently prevents the destruction of the melanocytes.[11] However, there are some controversial results in this case.

In the study of Khemis, *et al*., 30 patients with two bilateral lesions used PSD plus UVB in one of their lesions, whereas placebo plus UVB was applied to another lesion. The result showed no significant difference between control and case lesions.[12] Another study in which PSD was used in the literature came from Schallreuter and Rokos. They confirmed that PSD does not have the ability to diminish $H_2O_2$ form the skin under *in vitro* or *in vivo* conditions.[12] In another study with two case and control groups, which used narrow band UVB and narrow band UVB plus topical catalase-SOD, no superiority of treatment with PSD was shown.[8]

One of the potential drawbacks of this study was the lack of an objective measurement for repigmentation of vitiligous lesions. However, we tried our best to find a good method for an appropriate measurement of repigmentation. The use of digital morphometry or a colorimeter would allow more accurate and objective quantification of the differences in pigmentation following the treatment. On the other hand, our study has the advantage of having a self-control group which makes much more precise comparison and results possible.

In conclusion, this pilot study has shown that the topical use of PSD twice daily in combination with sun light exposure is not effective in vitiligo treatment. Larger studies with more appropriated objective repigmenting measurement are suggested.

## AUTHORS' CONTRIBUTION

All authors had active contributions in all stages of this study including data gathering, data analysis and manuscript preparation.

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**Source of Support:** This study was supported by the Vice-chancellery for Research of the Isfahan University of Medical Sciences.
**Conflict of Interest:** None declared.